

SEQUENCE LISTING

1020 Rec'd PCT/PTO 10 NOV 2005

<110> EXELIXIS, INC.

<120> MARKS AS MODIFIERS OF THE PTEN PATHWAY AND METHODS OF USE

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<150> US 60/479,768

<151> 2003-06-19

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<210> 14
 <211> 786
 <212> PRT
 <213> Homo sapiens

<400> 14

Met Val Ile Met Ser Glu Phe Ser Ala Asp Pro Ala Gly Gln Gly Gln
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Gly Gln Gln Lys Pro Leu Arg Val Gly Phe Tyr Asp Ile Glu Arg Thr
 20 25 30

Leu Gly Lys Gly Asn Phe Ala Val Val Lys Leu Ala Arg His Arg Val
 35 40 45

Thr Lys Thr Gln Val Ala Ile Lys Ile Ile Asp Lys Thr Arg Leu Asp
 50 55 60

Ser Ser Asn Leu Glu Lys Ile Tyr Arg Glu Val Gln Leu Met Lys Leu
 65 70 75 80

Leu Asn His Pro His Ile Ile Lys Leu Tyr Gln Val Met Glu Thr Lys
 85 90 95

Asp Met Leu Tyr Ile Val Thr Glu Phe Ala Lys Asn Gly Glu Met Phe
 100 105 110

Asp Tyr Leu Thr Ser Asn Gly His Leu Ser Glu Asn Glu Ala Arg Lys
 115 120 125

Lys Phe Trp Gln Ile Leu Ser Ala Val Glu Tyr Cys His Asp His His
 130 135 140

Ile Val His Arg Asp Leu Lys Thr Glu Asn Leu Leu Leu Asp Gly Asn
 145 150 155 160

Met Asp Ile Lys Leu Ala Gly Thr Glu Asp Phe Gly Phe Gly Asn Phe
 165 170 175

Tyr Lys Ser Gly Glu Pro Leu Ser Thr Trp Cys Gly Ser Pro Pro Tyr
 180 185 190

Ala Ala Pro Glu Val Phe Glu Gly Lys Glu Tyr Glu Gly Pro Gln Leu
 195 200 205

Asp Ile Trp Ser Leu Gly Val Val Leu Tyr Val Leu Val Cys Gly Ser

210	215	220
Leu Pro Phe Asp Gly Pro Asn Leu Pro Thr	Leu Arg Gln Arg Val Leu	
225	230	235 240
Glu Gly Arg Phe Arg Ile Pro Phe Phe Met Ser Gln Asp Cys Glu Ser		
245	250	255
Leu Ile Arg Arg Met Leu Val Val Asp Pro Ala Arg Arg Ile Thr Ile		
260	265	270
Ala Gln Ile Arg Gln His Arg Trp Met Arg Ala Glu Pro Cys Leu Pro		
275	280	285
Gly Pro Ala Cys Pro Ala Phe Ser Ala His Ser Tyr Thr Ser Asn Leu		
290	295	300
Gly Asp Tyr Asp Glu Gln Ala Leu Gly Ile Met Gln Thr Leu Gly Val		
305	310	315 320
Asp Arg Gln Arg Thr Val Glu Ser Leu Gln Asn Ser Ser Tyr Asn His		
325	330	335
Phe Ala Ala Ile Tyr Tyr Leu Leu Leu Glu Arg Leu Lys Glu Tyr Arg		
340	345	350
Asn Ala Gln Cys Ala Arg Pro Gly Pro Ala Arg Gln Pro Arg Pro Arg		
355	360	365
Ser Ser Asp Leu Ser Gly Leu Glu Val Pro Gln Glu Gly Leu Ser Thr		
370	375	380
Asp Pro Phe Arg Pro Ala Leu Leu Cys Pro Gln Pro Gln Thr Leu Val		
385	390	395 400
Gln Ser Val Leu Gln Ala Glu Met Asp Cys Glu Leu Gln Ser Ser Leu		
405	410	415
Gln Trp Pro Leu Phe Phe Pro Val Asp Ala Ser Cys Ser Gly Val Phe		
420	425	430
Arg Pro Arg Pro Val Ser Pro Ser Ser Leu Leu Asp Thr Ala Ile Ser		
435	440	445
Glu Glu Ala Arg Gln Gly Pro Gly Leu Glu Glu Glu Gln Asp Thr Gln		
450	455	460

Glu Ser Leu Pro Ser Ser Thr Gly Arg Arg His Thr Leu Ala Glu Val
 465 470 475 480

Ser Thr Arg Leu Ser Pro Leu Thr Ala Pro Cys Lys Phe Val Ser Pro
 485 490 495

Ser Thr Thr Ala Ser Pro Ala Glu Gly Thr Ser Ser Asp Ser Cys Leu
 500 505 510

Thr Phe Ser Ala Ser Lys Ser Pro Ala Gly Leu Ser Gly Thr Pro Ala
 515 520 525

Thr Gln Gly Leu Leu Gly Ala Cys Ser Pro Val Arg Leu Ala Ser Pro
 530 535 540

Phe Leu Gly Ser Gln Ser Ala Thr Pro Val Leu Gln Ala Gln Gly Gly
 545 550 555 560

Leu Gly Gly Ala Val Leu Leu Pro Val Ser Phe Gln Glu Gly Arg Arg
 565 570 575

Ala Ser Asp Thr Ser Leu Thr Gln Gly Leu Lys Ala Phe Arg Gln Gln
 580 585 590

Leu Arg Lys Thr Thr Arg Thr Lys Gly Phe Leu Gly Leu Asn Lys Ile
 595 600 605

Lys Gly Leu Ala Arg Gln Val Cys Gln Ala Pro Ala Ser Arg Ala Ser
 610 615 620

Arg Gly Gly Leu Ser Pro Phe His Ala Pro Ala Gln Ser Pro Gly Leu
 625 630 635 640

His Gly Gly Ala Ala Gly Ser Arg Glu Gly Trp Ser Leu Leu Glu Glu
 645 650 655

Val Leu Glu Gln Gln Arg Leu Leu Gln Leu Gln His His Pro Ala Ala
 660 665 670

Ala Pro Gly Cys Ser Gln Ala Pro Gln Pro Ala Pro Ala Pro Phe Val
 675 680 685

Ile Ala Pro Cys Asp Gly Pro Gly Ala Ala Pro Leu Pro Ser Thr Leu
 690 695 700

Leu Thr Ser Gly Leu Pro Leu Leu Pro Pro Pro Leu Leu Gln Thr Gly

705 710 715 720
 Ala Ser Pro Val Ala Ser Ala Ala Gln Leu Leu Asp Thr His Leu His
 725 730 735
 Ile Gly Thr Gly Pro Thr Ala Leu Pro Ala Val Pro Pro Pro Arg Leu
 740 745 750
 Ala Arg Leu Ala Pro Gly Cys Glu Pro Leu Gly Leu Leu Gln Gly Asp
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 Cys Glu Met Glu Asp Leu Met Pro Cys Ser Leu Gly Thr Phe Val Leu
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 Val Gln
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 Gly Gln Gln Lys Pro Leu Arg Val Gly Phe Tyr Asp Ile Glu Arg Thr
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 Leu Gly Lys Gly Asn Phe Ala Val Val Lys Leu Ala Arg His Arg Val
 35 40 45
 Thr Lys Thr Gln Val Ala Ile Lys Ile Ile Asp Lys Thr Arg Leu Asp
 50 55 60
 Ser Ser Asn Leu Glu Lys Ile Tyr Arg Glu Val Gln Leu Met Lys Leu
 65 70 75 80
 Leu Asn His Pro His Ile Ile Lys Leu Tyr Gln Val Met Glu Thr Lys
 85 90 95
 Asp Met Leu Tyr Ile Val Thr Glu Phe Ala Lys Asn Gly Glu Met Phe
 100 105 110
 Asp Tyr Leu Thr Ser Asn Gly His Leu Ser Glu Asn Glu Ala Arg Lys
 115 120 125

Lys Phe Trp Gln Ile Leu Ser Ala Val Glu Tyr Cys His Asp His His
 130 135 140
 Ile Val His Arg Asp Leu Lys Thr Glu Asn Leu Leu Leu Asp Gly Asn
 145 150 155 160
 Met Asp Ile Lys Leu Ala Asp Phe Gly Phe Gly Asn Phe Tyr Lys Ser
 165 170 175
 Gly Glu Pro Leu Ser Thr Trp Cys Gly Ser Pro Pro Tyr Ala Ala Pro
 180 185 190
 Glu Val Phe Glu Gly Lys Glu Tyr Glu Gly Pro Gln Leu Asp Ile Trp
 195 200 205
 Ser Leu Gly Val Val Leu Tyr Val Leu Val Cys Gly Ser Leu Pro Phe
 210 215 220
 Asp Gly Pro Asn Leu Pro Thr Leu Arg Gln Arg Val Leu Glu Gly Arg
 225 230 235 240
 Phe Arg Ile Pro Phe Phe Met Ser Gln Asp Cys Glu Ser Leu Ile Arg
 245 250 255
 Arg Met Leu Val Val Asp Pro Ala Arg Arg Ile Thr Ile Ala Gln Ile
 260 265 270
 Arg Gln His Arg Trp Met Arg Ala Glu Pro Cys Leu Pro Gly Pro Ala
 275 280 285
 Cys Pro Ala Phe Ser Ala His Ser Tyr Thr Ser Asn Leu Gly Asp Tyr
 290 295 300
 Asp Glu Gln Ala Leu Gly Ile Met Gln Thr Leu Gly Val Asp Arg Gln
 305 310 315 320
 Arg Thr Val Glu Ser Leu Gln Asn Ser Ser Tyr Asn His Phe Ala Ala
 325 330 335
 Ile Tyr Tyr Leu Leu Leu Glu Arg Leu Lys Glu Tyr Arg Asn Ala Gln
 340 345 350
 Cys Ala Arg Pro Gly Pro Ala Arg Gln Pro Arg Pro Arg Ser Ser Asp
 355 360 365
 Leu Ser Gly Leu Glu Val Pro Gln Glu Gly Leu Ser Thr Asp Pro Phe
 370 375 380

Arg Pro Ala Leu Leu Cys Pro Gln Pro Gln Thr Leu Val Gln Ser Val
385 390 395 400

Leu Gln Ala Glu Met Asp Cys Glu Leu Gln Ser Ser Leu Gln Trp Pro
405 410 415

Leu Phe Phe Pro Val Asp Ala Ser Cys Ser Gly Val Phe Arg Pro Arg
420 425 430

Pro Val Ser Pro Ser Ser Leu Leu Asp Thr Ala Ile Ser Glu Glu Ala
435 440 445

Arg Gln Gly Pro Gly Leu Glu Glu Glu Gln Asp Thr Gln Glu Ser Leu
450 455 460

Pro Ser Ser Thr Gly Arg Arg His Thr Leu Ala Glu Val Ser Thr Arg
465 470 475 480

Leu Ser Pro Leu Thr Ala Pro Cys Ile Val Val Ser Pro Ser Thr Thr
485 490 495

Ala Ser Pro Ala Glu Gly Thr Ser Ser Asp Ser Cys Leu Thr Phe Ser
500 505 510

Ala Ser Lys Ser Pro Ala Gly Leu Ser Gly Thr Pro Ala Thr Gln Gly
515 520 525

Leu Leu Gly Ala Cys Ser Pro Val Arg Leu Ala Ser Pro Phe Leu Gly
530 535 540

Ser Gln Ser Ala Thr Pro Val Leu Gln Ala Gln Gly Gly Leu Gly Gly
545 550 555 560

Ala Val Leu Leu Pro Val Ser Phe Gln Glu Gly Arg Arg Ala Ser Asp
565 570 575

Thr Ser Leu Thr Gln Gly Leu Lys Ala Phe Arg Gln Gln Leu Arg Lys
580 585 590

Thr Thr Arg Thr Lys Gly Phe Leu Gly Leu Asn Lys Ile Lys Gly Leu
595 600 605

Ala Arg Gln Val Cys Gln Val Pro Ala Ser Arg Ala Ser Arg Gly Gly
610 615 620

Leu Ser Pro Phe His Ala Pro Ala Gln Ser Pro Gly Leu His Gly Gly
625 630 635 640

Ala Ala Gly Ser Arg Glu Gly Trp Ser Leu Leu Glu Glu Val Leu Glu
645 650 655

Gln Gln Arg Leu Leu Gln Leu Gln His His Pro Ala Ala Ala Pro Gly
660 665 670

Cys Ser Gln Ala Pro Gln Pro Ala Pro Ala Pro Phe Val Ile Ala Pro
675 680 685

Cys Asp Gly Pro Gly Ala Ala Pro Leu Pro Ser Thr Leu Leu Thr Ser
690 695 700

Gly Leu Pro Leu Leu Pro Pro Pro Leu Leu Gln Thr Gly Ala Ser Pro
705 710 715 720

Val Ala Ser Ala Ala Gln Leu Leu Asp Thr His Leu His Ile Gly Thr
725 730 735

Gly Pro Thr Ala Leu Pro Ala Val Pro Pro Pro Arg Leu Ala Arg Leu
740 745 750

Ala Pro Gly Cys Glu Pro Leu Gly Leu Leu Gln Gly Asp Cys Glu Met
755 760 765

Glu Asp Leu Met Pro Cys Ser Leu Gly Thr Phe Val Leu Val Gln
770 775 780

<210> 16
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<212> PRT
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<400> 16

Ala Gln Gly Trp Gln Ala Val Gly Thr Gly Ala Arg Ala Ser Ala Val
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Ala Ala Val Pro Ser Val Ser Leu Leu Ser Gly Ala Ser Ser Ser Ser
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Leu Ala Trp Cys Gly Leu Ala Thr Gly Ala Leu Gly Ala Gly Ala Arg
35 40 45

Gly Ile Pro Glu Leu Arg Gly Ala Ala Gly Ala Gly Gly Ala Ala Gly
50 55 60

Ala Gly Thr Gly Gly Ala Gly Pro Ala Gly Arg Leu Leu Pro Pro Pro
 65 70 75 80

Ala Pro Gly Ser Pro Ala Ala Pro Ala Ala Val Ser Pro Ala Ala Gly
 85 90 95

Gln Pro Arg Pro Pro Ala Pro Ala Ser Arg Gly Pro Met Pro Ala Arg
 100 105 110

Ile Gly Tyr Tyr Glu Ile Asp Arg Thr Ile Gly Lys Gly Asn Phe Ala
 115 120 125

Val Val Lys Arg Ala Thr His Leu Val Thr Lys Ala Lys Val Ala Ile
 130 135 140

Lys Ile Ile Asp Lys Thr Gln Leu Asp Glu Glu Asn Leu Lys Lys Ile
 145 150 155 160

Phe Arg Glu Val Gln Ile Met Lys Met Leu Cys His Pro His Ile Ile
 165 170 175

Arg Leu Tyr Gln Val Met Glu Thr Glu Arg Met Ile Tyr Leu Val Thr
 180 185 190

Glu Tyr Ala Ser Gly Gly Glu Ile Phe Asp His Leu Val Ala His Gly
 195 200 205

Arg Met Ala Glu Lys Glu Ala Arg Arg Lys Phe Lys Gln Ile Val Thr
 210 215 220

Ala Val Tyr Phe Cys His Cys Arg Asn Ile Val His Arg Asp Leu Lys
 225 230 235 240

Ala Glu Asn Leu Leu Leu Asp Ala Asn Leu Asn Ile Lys Ile Ala Asp
 245 250 255

Phe Gly Phe Ser Asn Leu Phe Thr Pro Gly Gln Leu Leu Lys Thr Trp
 260 265 270

Cys Gly Ser Pro Pro Tyr Ala Ala Pro Glu Leu Phe Glu Gly Lys Glu
 275 280 285

Tyr Asp Gly Pro Lys Val Asp Ile Trp Ser Leu Gly Val Val Leu Tyr
 290 295 300

Val Leu Val Cys Gly Ala Leu Pro Phe Asp Gly Ser Thr Leu Gln Asn

305	310	315	320
Leu Arg Ala Arg Val Leu Ser Gly Lys Phe Arg Ile Pro Phe Phe Met	325	330	335
Ser Thr Glu Cys Glu His Leu Ile Arg His Met Leu Val Leu Asp Pro	340	345	350
Asn Lys Arg Leu Ser Met Glu Gln Ile Cys Lys His Lys Trp Met Lys	355	360	365
Leu Gly Asp Ala Asp Pro Asn Phe Asp Arg Leu Ile Ala Glu Cys Gln	370	375	380
Gln Leu Lys Glu Glu Arg Gln Val Asp Pro Leu Asn Glu Asp Val Leu	385	390	395
Leu Ala Met Glu Asp Met Gly Leu Asp Lys Glu Gln Thr Leu Gln Ser	405	410	415
Leu Arg Ser Asp Ala Tyr Asp His Tyr Ser Ala Ile Tyr Ser Leu Leu	420	425	430
Cys Asp Arg His Lys Arg His Lys Thr Leu Arg Leu Gly Ala Leu Pro	435	440	445
Ser Met Pro Arg Ala Leu Ala Phe Gln Ala Pro Val Asn Ile Gln Ala	450	455	460
Glu Gln Ala Gly Thr Ala Met Asn Ile Ser Val Pro Gln Val Gln Leu	465	470	475
Ile Asn Pro Glu Asn Gln Ile Val Glu Pro Asp Gly Thr Leu Asn Leu	485	490	495
Asp Ser Asp Glu Gly Glu Glu Pro Ser Pro Glu Ala Leu Val Arg Tyr	500	505	510
Leu Ser Met Arg Arg His Thr Val Gly Val Ala Asp Pro Arg Thr Glu	515	520	525
Val Met Glu Asp Leu Gln Lys Leu Leu Pro Gly Phe Pro Gly Val Asn	530	535	540
Pro Gln Ala Pro Phe Leu Gln Val Ala Pro Asn Val Asn Phe Met His	545	550	555
			560

Asn Leu Leu Pro Met Gln Asn Leu Gln Pro Thr Gly Gln Leu Glu Tyr
 565 570 575

Lys Glu Gln Ser Leu Leu Gln Pro Pro Thr Leu Gln Leu Leu Asn Gly
 580 585 590

Met Gly Pro Leu Gly Arg Arg Ala Ser Asp Gly Gly Ala Asn Ile Gln
 595 600 605

Leu His Ala Gln Gln Leu Leu Lys Arg Pro Arg Gly Pro Ser Pro Leu
 610 615 620

Val Thr Met Thr Pro Ala Val Pro Ala Val Thr Pro Val Asp Glu Glu
 625 630 635 640

Ser Ser Asp Gly Glu Pro Asp Gln Glu Ala Val Gln Ser Ser Thr Tyr
 645 650 655

Lys Asp Ser Asn Thr Leu His Leu Pro Thr Glu Arg Phe Ser Pro Val
 660 665 670

Arg Arg Phe Ser Asp Gly Ala Ala Ser Ile Gln Ala Phe Lys Ala His
 675 680 685

Leu Glu Lys Met Gly Asn Asn Ser Ser Ile Lys Gln Leu Gln Gln Glu
 690 695 700

Cys Glu Gln Leu Gln Lys Met Tyr Gly Gly Gln Ile Asp Glu Arg Thr
 705 710 715 720

Leu Glu Lys Thr Gln Gln Gln His Met Leu Tyr Gln Gln Glu Gln His
 725 730 735

His Gln Ile Leu Gln Gln Gln Ile Gln Asp Ser Ile Cys Pro Pro Gln
 740 745 750

Pro Ser Pro Pro Leu Gln Ala Ala Cys Glu Asn Gln Pro Ala Leu Leu
 755 760 765

Thr His Gln Leu Gln Arg Leu Arg Ile Gln Pro Ser Ser Pro Pro Pro
 770 775 780

Asn His Pro Asn Asn His Leu Phe Arg Gln Pro Ser Asn Ser Pro Pro
 785 790 795 800

Pro Met Ser Ser Ala Met Ile Gln Pro His Gly Ala Ala Ser Ser Ser

805

810

815

Gln Phe Gln Gly Leu Pro Ser Arg Ser Ala Ile Phe Gln Gln Gln Pro
 820 825 830

Glu Asn Cys Ser Ser Pro Pro Asn Val Ala Leu Thr Cys Leu Gly Met
 835 840 845

Gln Gln Pro Ala Gln Ser Gln Gln Val Thr Ile Gln Val Gln Glu Pro
 850 855 860

Val Asp Met Leu Ser Asn Met Pro Gly Thr Ala Ala Gly Ser Ser Gly
 865 870 875 880

Arg Gly Ile Ser Ile Ser Pro Ser Ala Gly Gln Met Gln Met Gln His
 885 890 895

Arg Thr Asn Leu Met Ala Thr Leu Ser Tyr Gly His Arg Pro Leu Ser
 900 905 910

Lys Gln Leu Ser Ala Asp Ser Ala Glu Ala His Ser Leu Asn Val Asn
 915 920 925

Arg Phe Ser Pro Ala Asn Tyr Asp Gln Ala His Leu His Pro His Leu
 930 935 940

Phe Ser Asp Gln Ser Arg Gly Ser Pro Ser Ser Tyr Ser Pro Ser Thr
 945 950 955 960

Gly Val Gly Phe Ser Pro Thr Gln Ala Leu Lys Val Pro Pro Leu Asp
 965 970 975

Gln Phe Pro Thr Phe Pro Pro Ser Ala His Gln Gln Pro Pro His Tyr
 980 985 990

Thr Thr Ser Ala Leu Gln Gln Ala Leu Leu Ser Pro Thr Pro Pro Asp
 995 1000 1005

Tyr Thr Arg His Gln Gln Val Pro His Ile Leu Gln Gly Leu Leu
 1010 1015 1020

Ser Pro Arg His Ser Leu Thr Gly His Ser Asp Ile Arg Leu Pro
 1025 1030 1035

Pro Thr Glu Phe Ala Gln Leu Ile Lys Arg Gln Gln Gln Gln Arg
 1040 1045 1050

Gln Gln Gln Gln Gln Gln Gln Gln Gln Glu Tyr Gln Glu Leu
 1055 1060 1065

Phe Arg His Met Asn Gln Gly Asp Ala Gly Ser Leu Ala Pro Ser
 1070 1075 1080

Leu Gly Gly Gln Ser Met Thr Glu Arg Gln Ala Leu Ser Tyr Gln
 1085 1090 1095

Asn Ala Asp Ser Tyr His His His Thr Ser Pro Gln His Leu Leu
 1100 1105 1110

Gln Ile Arg Ala Gln Glu Cys Val Ser Gln Ala Ser Ser Pro Thr
 1115 1120 1125

Pro Pro His Gly Tyr Ala His Gln Pro Ala Leu Met His Ser Glu
 1130 1135 1140

Ser Met Glu Glu Asp Cys Ser Cys Glu Gly Ala Lys Asp Gly Phe
 1145 1150 1155

Gln Asp Ser Lys Ser Ser Ser Thr Leu Thr Lys Gly Cys His Asp
 1160 1165 1170

Ser Pro Leu Leu Leu Ser Thr Gly Gly Pro Gly Asp Pro Glu Ser
 1175 1180 1185

Leu Leu Gly Thr Val Ser His Ala Gln Glu Leu Gly Ile His Pro
 1190 1195 1200

Tyr Gly His Gln Pro Thr Ala Ala Phe Ser Lys Asn Lys Val Pro
 1205 1210 1215

Ser Arg Glu Pro Val Ile Gly Asn Cys Met Asp Arg Ser Ser Pro
 1220 1225 1230

Gly Gln Ala Val Glu Leu Pro Asp His Asn Gly Leu Gly Tyr Pro
 1235 1240 1245

Ala Arg Pro Ser Val His Glu His His Arg Pro Arg Ala Leu Gln
 1250 1255 1260

Arg His His Thr Ile Gln Asn Ser Asp Asp Ala Tyr Val Gln Leu
 1265 1270 1275

Asp Asn Leu Pro Gly Met Ser Leu Val Ala Gly Lys Ala Leu Ser

1280

1285

1290

Ser Ala Arg Met Ser Asp Ala Val Leu Ser Gln Ser Ser Leu Met
 1295 1300 1305

Gly Ser Gln Gln Phe Gln Asp Gly Glu Asn Glu Glu Cys Gly Ala
 1310 1315 1320

Ser Leu Gly Gly His Glu His Pro Asp Leu Ser Asp Gly Ser Gln
 1325 1330 1335

His Leu Asn Ser Ser Cys Tyr Pro Ser Thr Cys Ile Thr Asp Ile
 1340 1345 1350

Leu Leu Ser Tyr Lys His Pro Glu Val Ser Phe Ser Met Glu Gln
 1355 1360 1365

Ala Gly Val
 1370

<210> 17
 <211> 926
 <212> PRT
 <213> Homo sapiens

<400> 17

Met Val Met Ala Asp Gly Pro Arg His Leu Gln Arg Gly Pro Val Arg
 1 5 10 15

Val Gly Phe Tyr Asp Ile Glu Gly Thr Leu Gly Lys Gly Asn Phe Ala
 20 25 30

Val Val Lys Leu Gly Arg His Arg Ile Thr Lys Thr Glu Val Ala Ile
 35 40 45

Lys Ile Ile Asp Lys Ser Gln Leu Asp Ala Val Asn Leu Glu Lys Ile
 50 55 60

Tyr Arg Glu Val Gln Ile Met Lys Met Leu Asp His Pro His Ile Ile
 65 70 75 80

Lys Leu Tyr Gln Val Met Glu Thr Lys Ser Met Leu Tyr Leu Val Thr
 85 90 95

Glu Tyr Ala Lys Asn Gly Glu Ile Phe Asp Tyr Leu Ala Asn His Gly
 100 105 110

Arg Leu Asn Glu Ser Glu Ala Arg Arg Lys Phe Trp Gln Ile Leu Ser
 115 120 125

Ala Val Asp Tyr Cys His Gly Arg Lys Ile Val His Arg Asp Leu Lys
 130 135 140

Ala Glu Asn Leu Leu Leu Asp Asn Asn Met Asn Ile Lys Ile Ala Asp
 145 150 155 160

Phe Gly Phe Gly Asn Phe Phe Lys Ser Gly Glu Leu Leu Ala Thr Trp
 165 170 175

Cys Gly Ser Pro Pro Tyr Ala Ala Pro Glu Val Phe Glu Gly Gln Gln
 180 185 190

Tyr Glu Gly Pro Gln Leu Asp Ile Trp Ser Met Gly Val Val Leu Tyr
 195 200 205

Val Leu Val Cys Gly Ala Leu Pro Phe Asp Gly Pro Thr Leu Pro Ile
 210 215 220

Leu Arg Gln Arg Val Leu Glu Gly Arg Phe Arg Ile Pro Tyr Phe Met
 225 230 235 240

Ser Glu Asp Cys Glu His Leu Ile Arg Arg Met Leu Val Leu Asp Pro
 245 250 255

Ser Lys Arg Leu Thr Ile Ala Gln Ile Lys Glu His Lys Trp Met Leu
 260 265 270

Ile Glu Val Pro Val Gln Arg Pro Val Leu Tyr Pro Gln Glu Gln Glu
 275 280 285

Asn Glu Pro Ser Ile Gly Glu Phe Asn Glu Gln Val Leu Arg Leu Met
 290 295 300

His Ser Leu Gly Ile Asp Gln Gln Lys Thr Ile Glu Ser Leu Gln Asn
 305 310 315 320

Lys Ser Tyr Asn His Phe Ala Ala Ile Tyr Phe Leu Leu Val Glu Arg
 325 330 335

Leu Lys Ser His Arg Ser Ser Phe Pro Val Glu Gln Arg Leu Asp Gly
 340 345 350

Arg Gln Arg Arg Pro Ser Thr Ile Ala Glu Gln Thr Val Ala Lys Ala
 355 360 365

Gln Thr Val Gly Leu Pro Val Thr Met His Ser Pro Asn Met Arg Leu
 370 375 380

Leu Arg Ser Ala Leu Leu Pro Gln Ala Ser Asn Val Glu Ala Phe Ser
 385 390 395 400

Phe Pro Ala Ser Gly Cys Gln Ala Glu Ala Ala Phe Met Glu Glu Glu
 405 410 415

Cys Val Asp Thr Pro Lys Val Asn Gly Cys Leu Leu Asp Pro Val Pro
 420 425 430

Pro Val Leu Val Arg Lys Gly Cys Gln Ser Leu Pro Ser Asn Met Met
 435 440 445

Glu Thr Ser Ile Asp Glu Gly Leu Glu Thr Glu Gly Glu Ala Glu Glu
 450 455 460

Asp Pro Ala His Ala Phe Glu Ala Phe Gln Ser Thr Arg Ser Gly Gln
 465 470 475 480

Arg Arg His Thr Leu Ser Glu Val Thr Asn Gln Leu Val Val Met Pro
 485 490 495

Gly Ala Gly Lys Ile Phe Ser Met Asn Asp Ser Pro Ser Leu Asp Ser
 500 505 510

Val Asp Ser Glu Tyr Asp Met Gly Ser Val Gln Arg Asp Leu Asn Phe
 515 520 525

Leu Glu Asp Asn Pro Ser Leu Lys Asp Ile Met Leu Ala Asn Gln Pro
 530 535 540

Ser Pro Arg Met Thr Ser Pro Phe Ile Ser Leu Arg Pro Thr Asn Pro
 545 550 555 560

Ala Met Gln Ala Leu Ser Ser Gln Lys Arg Glu Val His Asn Arg Ser
 565 570 575

Pro Val Ser Phe Arg Glu Gly Arg Arg Ala Ser Asp Thr Ser Leu Thr
 580 585 590

Gln Gly Ile Val Ala Phe Arg Gln His Leu Gln Asn Leu Ala Arg Thr
 595 600 605

Lys Gly Ile Leu Glu Leu Asn Lys Val Gln Leu Leu Tyr Glu Gln Ile
 610 615 620

Gly Pro Glu Ala Asp Pro Asn Leu Ala Pro Ala Ala Pro Gln Leu Gln
 625 630 635 640

Asp Leu Ala Ser Ser Cys Pro Gln Glu Glu Val Ser Gln Gln Gln Glu
 645 650 655

Ser Val Ser Thr Leu Pro Ala Ser Val His Pro Gln Leu Ser Pro Arg
 660 665 670

Gln Ser Leu Glu Thr Gln Tyr Leu Gln His Arg Leu Gln Lys Pro Ser
 675 680 685

Leu Leu Ser Lys Ala Gln Asn Thr Cys Gln Leu Tyr Cys Lys Glu Pro
 690 695 700

Pro Arg Ser Leu Glu Gln Gln Leu Gln Glu His Arg Leu Gln Gln Lys
 705 710 715 720

Arg Leu Phe Leu Gln Lys Gln Ser Gln Leu Gln Ala Tyr Phe Asn Gln
 725 730 735

Met Gln Ile Ala Glu Ser Ser Tyr Pro Gln Pro Ser Gln Gln Leu Pro
 740 745 750

Leu Pro Arg Gln Glu Thr Pro Pro Pro Ser Gln Gln Ala Pro Pro Phe
 755 760 765

Ser Leu Thr Gln Pro Leu Ser Pro Val Leu Glu Pro Ser Ser Glu Gln
 770 775 780

Met Gln Tyr Ser Pro Phe Leu Ser Gln Tyr Gln Glu Met Gln Leu Gln
 785 790 795 800

Pro Leu Pro Ser Thr Ser Gly Pro Arg Ala Ala Pro Pro Leu Pro Thr
 805 810 815

Gln Leu Gln Gln Gln Gln Pro Pro Pro Pro Pro Pro Pro Pro Pro
 820 825 830

Arg Gln Pro Gly Ala Ala Pro Ala Pro Leu Gln Phe Ser Tyr Gln Thr
 835 840 845

Cys Glu Leu Pro Ser Ala Ala Ser Pro Ala Pro Asp Tyr Pro Thr Pro
 850 855 860

Cys Gln Tyr Pro Val Asp Gly Ala Gln Gln Ser Asp Leu Thr Gly Pro
865 870 875 880

Asp Cys Pro Arg Ser Pro Gly Leu Gln Glu Ala Pro Ser Ser Tyr Asp
885 890 895

Pro Leu Ala Leu Ser Glu Leu Pro Gly Leu Phe Asp Cys Glu Met Leu
900 905 910

Asp Ala Val Asp Pro Gln His Asn Gly Tyr Val Leu Val Asn
915 920 925

<210> 18

<211> 926

<212> PRT

<213> Homo sapiens

<400> 18

Met Val Met Ala Asp Gly Pro Arg His Leu Gln Arg Gly Pro Val Arg
1 5 10 15

Val Gly Phe Tyr Asp Ile Glu Gly Thr Leu Gly Lys Gly Asn Phe Ala
20 25 30

Val Val Lys Leu Gly Arg His Arg Ile Thr Lys Thr Glu Val Ala Ile
35 40 45

Lys Ile Ile Asp Lys Ser Gln Leu Asp Ala Val Asn Leu Glu Lys Ile
50 55 60

Tyr Arg Glu Val Gln Ile Met Lys Met Leu Asp His Pro His Ile Ile
65 70 75 80

Lys Leu Tyr Gln Val Met Glu Thr Lys Ser Met Leu Tyr Leu Val Thr
85 90 95

Glu Tyr Ala Lys Asn Gly Glu Ile Phe Asp Tyr Leu Ala Asn His Gly
100 105 110

Arg Leu Asn Glu Ser Glu Ala Arg Arg Lys Phe Trp Gln Ile Leu Ser
115 120 125

Ala Val Asp Tyr Cys His Gly Arg Lys Ile Val His Arg Asp Leu Lys
130 135 140

Ala Glu Asn Leu Leu-Leu Asp Asn Asn Met Asn Ile Lys Ile Ala Asp

145 150 155 160
 Phe Gly Phe Gly Asn Phe Phe Lys Ser Gly Glu Leu Leu Ala Thr Trp
 165 170 175
 Cys Gly Ser Pro Pro Tyr Ala Ala Pro Glu Val Phe Glu Gly Gln Gln
 180 185 190
 Tyr Glu Gly Pro Gln Leu Asp Ile Trp Ser Met Gly Val Val Leu Tyr
 195 200 205
 Val Leu Val Cys Gly Ala Leu Pro Phe Asp Gly Pro Thr Leu Pro Ile
 210 215 220
 Leu Arg Gln Arg Val Leu Glu Gly Arg Phe Arg Ile Pro Tyr Phe Met
 225 230 235 240
 Ser Glu Asp Cys Glu His Leu Ile Arg Arg Met Leu Val Leu Asp Pro
 245 250 255
 Ser Lys Arg Leu Thr Ile Ala Gln Ile Lys Glu His Lys Trp Met Leu
 260 265 270
 Ile Glu Val Pro Val Gln Arg Pro Val Leu Tyr Pro Gln Glu Gln Glu
 275 280 285
 Asn Glu Pro Ser Ile Gly Glu Phe Asn Glu Gln Val Leu Arg Leu Met
 290 295 300
 His Ser Leu Gly Ile Asp Gln Gln Lys Thr Ile Glu Ser Leu Gln Asn
 305 310 315 320
 Lys Ser Tyr Asn His Phe Ala Ala Ile Tyr Phe Leu Leu Val Glu Arg
 325 330 335
 Leu Lys Ser His Arg Ser Ser Phe Pro Val Glu Gln Arg Leu Asp Gly
 340 345 350
 Arg Gln Arg Arg Pro Ser Thr Ile Ala Glu Gln Thr Val Ala Lys Ala
 355 360 365
 Gln Thr Val Gly Leu Pro Val Thr Met His Ser Pro Asn Met Arg Leu
 370 375 380
 Leu Arg Ser Ala Leu Leu Pro Gln Ala Ser Asn Val Glu Ala Phe Ser
 385 390 395 400

Phe Pro Ala Ser Gly Cys Gln Ala Glu Ala Ala Phe Met Glu Glu Glu
405 410 415

Cys Val Asp Thr Pro Lys Val Asn Gly Cys Leu Leu Asp Pro Val Pro
420 425 430

Pro Val Leu Val Arg Lys Gly Cys Gln Ser Leu Pro Ser Asn Met Met
435 440 445

Glu Thr Ser Ile Asp Glu Gly Leu Glu Thr Glu Gly Glu Ala Glu Glu
450 455 460

Asp Pro Ala His Ala Phe Glu Ala Phe Gln Ser Thr Arg Ser Gly Gln
465 470 475 480

Arg Arg His Thr Leu Ser Glu Val Thr Asn Gln Leu Val Val Met Pro
485 490 495

Gly Ala Gly Lys Ile Phe Ser Met Asn Asp Ser Pro Ser Leu Asp Ser
500 505 510

Val Asp Ser Glu Tyr Asp Met Gly Ser Val Gln Arg Asp Leu Asn Phe
515 520 525

Leu Glu Asp Asn Pro Ser Leu Lys Asp Ile Met Leu Ala Asn Gln Pro
530 535 540

Ser Pro Arg Met Thr Ser Pro Phe Ile Ser Leu Arg Pro Thr Asn Pro
545 550 555 560

Ala Met Gln Ala Leu Ser Ser Gln Lys Arg Glu Val His Asn Arg Ser
565 570 575

Pro Val Ser Phe Arg Glu Gly Arg Arg Ala Ser Asp Thr Ser Leu Thr
580 585 590

Gln Gly Ile Val Ala Phe Arg Gln His Leu Gln Asn Leu Ala Arg Thr
595 600 605

Lys Gly Ile Leu Glu Leu Asn Lys Val Gln Leu Leu Tyr Glu Gln Ile
610 615 620

Gly Pro Glu Ala Asp Pro Asn Leu Ala Pro Ala Ala Pro Gln Leu Gln
625 630 635 640

Asp Leu Ala Ser Ser Cys Pro Gln Glu Glu Val Ser Gln Gln Gln Glu

645

650

655

Ser Val Ser Thr Leu Pro Ala Ser Val His Pro Gln Leu Ser Pro Arg
660 665 670

Gln Ser Leu Glu Thr Gln Tyr Leu Gln His Arg Leu Gln Lys Pro Ser
675 680 685

Leu Leu Ser Lys Ala Gln Asn Thr Cys Gln Leu Tyr Cys Lys Glu Pro
690 695 700

Pro Arg Ser Leu Glu Gln Gln Leu Gln Glu His Arg Leu Gln Gln Lys
705 710 715 720

Arg Leu Phe Leu Gln Lys Gln Ser Gln Leu Gln Ala Tyr Phe Asn Gln
725 730 735

Met Gln Ile Ala Glu Ser Ser Tyr Pro Gln Pro Ser Gln Gln Leu Pro
740 745 750

Leu Pro Arg Gln Glu Thr Pro Pro Pro Ser Gln Gln Ala Pro Pro Phe
755 760 765

Ser Leu Thr Gln Pro Leu Ser Pro Val Leu Glu Pro Ser Ser Glu Gln
770 775 780

Met Gln Tyr Ser Pro Phe Leu Ser Gln Tyr Gln Glu Met Gln Leu Gln
785 790 795 800

Pro Leu Pro Ser Thr Ser Gly Pro Arg Ala Ala Pro Pro Leu Pro Thr
805 810 815

Gln Leu Gln Gln Gln Gln Pro Pro Pro Pro Pro Pro Pro Pro Pro
820 825 830

Arg Gln Pro Gly Ala Ala Pro Ala Pro Leu Gln Phe Ser Tyr Gln Thr
835 840 845

Cys Glu Leu Pro Ser Ala Ala Ser Pro Ala Pro Asp Tyr Pro Thr Pro
850 855 860

Cys Gln Tyr Pro Val Asp Gly Ala Gln Gln Ser Asp Leu Thr Gly Pro
865 870 875 880

Asp Cys Pro Arg Ser Pro Gly Leu Gln Glu Ala Pro Ser Ser Tyr Asp
885 890 895

Pro Leu Ala Leu Ser Glu Leu Pro Gly Leu Phe Asp Cys Glu Met Leu
900 905 910

Asp Ala Val Asp Pro Gln His Asn Gly Tyr Val Leu Val Asn
915 920 925